

ORIGINAL PAPER

## SURGICAL MANAGEMENT OF PATIENTS WITH RECTAL NEOPLASTIC DISEASE – PREDICTION FACTORS IN LOW ANTERIOR RESECTION SYNDROME

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### ABSTRACT

**The objective of the study** Rectal cancer represents a public health issue, considering the increased incidence among the general population in Romania. At present, the ideal management of patients diagnosed with rectal neoplasms, leading to oncological healing while preserving all physiological functions, includes the low anterior resection of the rectum (LARS) with the partial or total excision of the mesorectum. The aim of the paper is to analyze the physiological, psychological and oncological impact of surgical intervention on patients diagnosed with rectal cancer.

**Material and methods** Our study was retrospective, observational, descriptive, unicentric, and took place in the General Surgery and Emergency Clinic III<sup>rd</sup> of the Bucharest University Emergency Hospital, Romania, during 1 January, 2005 –31 December, 2016. The study included a total of 92 patients.

**Results** The values of LARS score ranged from 0-42. The mean LARS scores in the study group were 12.46 with a median of 7 and a 13.06 standard deviation.

**Conclusions** The distance from the anastomosis level to the pectinate line, side-to-end anastomosis, the impossibility to identify the nerves, the occurrence of anastomotic fistula are predictive factors for the occurrence of major LARS during post-surgery evolution.

### RÉSUMÉ

**Approche chirurgicale des patients avec cancer rectal – facteurs prédictifs du syndrome de la résection antérieure basse**

**L'objectif de l'étude** Le cancer rectal représente un problème de santé publique, compte tenu de l'incidence accrue dans la population générale en Roumanie. Actuellement, la prise en charge idéale des patients diagnostiqués avec des néoplasies rectales, conduisant à une cicatrisation oncologique tout en préservant toutes les fonctions physiologiques, comprend la résection antérieure du rectum avec excision partielle ou totale du mésorectum. Le but de cet article est d'analyser l'impact physiologique, psychologique et oncologique de l'intervention chirurgicale chez les patients diagnostiqués avec un cancer du rectum.

**Matériel et méthodes** Notre étude était rétrospective, observationnelle, descriptive, unicentrique et a eu lieu à la Clinique de chirurgie générale et d'urgence III de l'Hôpital d'Urgence de l'Université de Bucarest du 1er janvier 2005 au 31 décembre 2016 et a inclus un total de 92 patients.

**Résultats** Les valeurs du score LARS ont des valeurs comprises entre 0 et 42. Les scores LARS moyens dans le groupe d'étude étaient de 12,46 avec une médiane de 7 et un écart-type de 13,06.

**Key words:** rectal cancer, low anterior resection, colo-rectal anastomosis.

**Conclusions** La distance du niveau d'anastomose à la ligne de pectinate, anastomose de bout en bout, l'impossibilité d'identifier le nerf, l'apparition de la fistule anastomotique sont des facteurs prédictifs de la survenue de LARS majeurs au cours de l'évolution post-opératoire.

**Mots clés:** cancer rectal, résection antérieure basse, anastomose colorectale.

## INTRODUCTION

Rectal cancer represents a public health issue, considering the increased incidence among the general population in Romania. The delayed diagnosis led, until recently, to reduced possibilities in terms of therapeutic options and healing, with a predominantly palliative management of these patients. The development of modern diagnostic techniques, as well as the increase of patients' addressability to specialized health care facilities, led to the possibility of establishing an early diagnosis for a growing number of patients, which allowed the evolution of oncological management and desideratum towards a curative attitude in the majority of patients<sup>1</sup>.

At present, the ideal management of patients diagnosed with rectal neoplasms, leading to oncological healing while preserving all physiological functions, includes the anterior resection of the rectum, with the partial or total excision of the mesorectum. During this procedure, it is the colorectal anastomosis that allows the continuity of the digestive tract for the complete preservation of the digestive function<sup>2,3</sup>.

The group of complications that often follow this surgical technique, from a digestive point of view - incontinence, urgency and frequency of defecation, has been reunited over the last few years under the name of Low Anterior Resection Syndrome - LARS. Practitioners' attention has been focused on factors that may condition or predict the occurrence of this syndrome, in order to identify optimal therapeutic attitudes and achieve an increased quality of patients' lives<sup>4,5</sup>.

As a corollary of the aforementioned, a very important element regarding the observance of the professional ethics component is that the patient is the one who, according to the legislation in force and with the ethical principles, can decide on which option of treatment to be applied. The physician is required to provide the patient with all the elements regarding the prognosis, risks, nature and purpose of the proposed medical act, the interventions and the proposed therapeutic strategy, the benefits and consequences of the intervention, viable alternatives

to treatment and their risks, the risks of not having the intervention, as well as the risks associated with non-following medical recommendations. Following the above, the patient decides the treatment option and gives his consent by signing the Informed Consent, a binding document to prevent a possible malpractice charge.

The present study has been based on the observation that the increased incidence of rectal cancer in Romania should determine us to study the optimal therapeutic options for patients with this pathology, even in advanced cases, in order to accurately and fully inform the risks of developing some postoperative complications.

**THE AIM** of the paper is to analyze the physiological, psychological and oncological impact of surgical intervention on patients diagnosed with rectal cancer.

## MATERIAL AND METHOD

Our study was retrospective, observative, descriptive, unicentric and took place at the General Surgery and Emergency Clinic IIIrd of the Bucharest University Emergency Hospital during 1 January, 2005 -31 December, 2016. The study included a total of 92 patients.

Good conduct in research has been provided in accordance with international regulations in the field, legislation and ethical rules of scientific research.

Agreement has been obtained from competent authorities in order to access patients' observation sheets and operator protocols.

Inclusion criteria:

1. Patients whose diagnosis at discharge was of rectal neoplasm and whose surgical treatment was carried out in General Surgery and Emergency III Clinic.
2. Existence in observation sheets and operative documents of all parameters necessary for evaluation of the patient with rectal neoplasm, according to the established protocol.

3. Existence in the analyzed medical documents of data on the immediate and late post-operative evolution, from the perspective of the occurrence of complications.
4. Patients with a minimum age of 18 years.
 

Exclusion criteria:

  1. Patients admitted to the General Surgery and Emergency IIIrd Clinic, where palliative surgery was performed.
  2. Patients who were hospitalized and eventually initially operated in another health facility, with no accurate evidence of the preoperative assessment and therapeutic attitude prior to their transfer to the clinic where the research was conducted.
  3. Patients hospitalized and/or operated from the beginning in the General Surgery and Emergency IIIrd Clinic of the University Emergency Hospital, Bucharest, with the diagnosis of rectal neoplasm, but in whom there is no exact evidence of the quantified parameters or the remote monitoring of the complications of the surgical intervention.
  4. Patients with limited resections.

## RESULTS

From the point of view of the distance, estimated intraoperatively, between the anastomosis and the pectinate line in the group of patients undergoing resection, the results have shown an average value of 6.76 cm (values ranging from 1-10 cm) (Table 1).

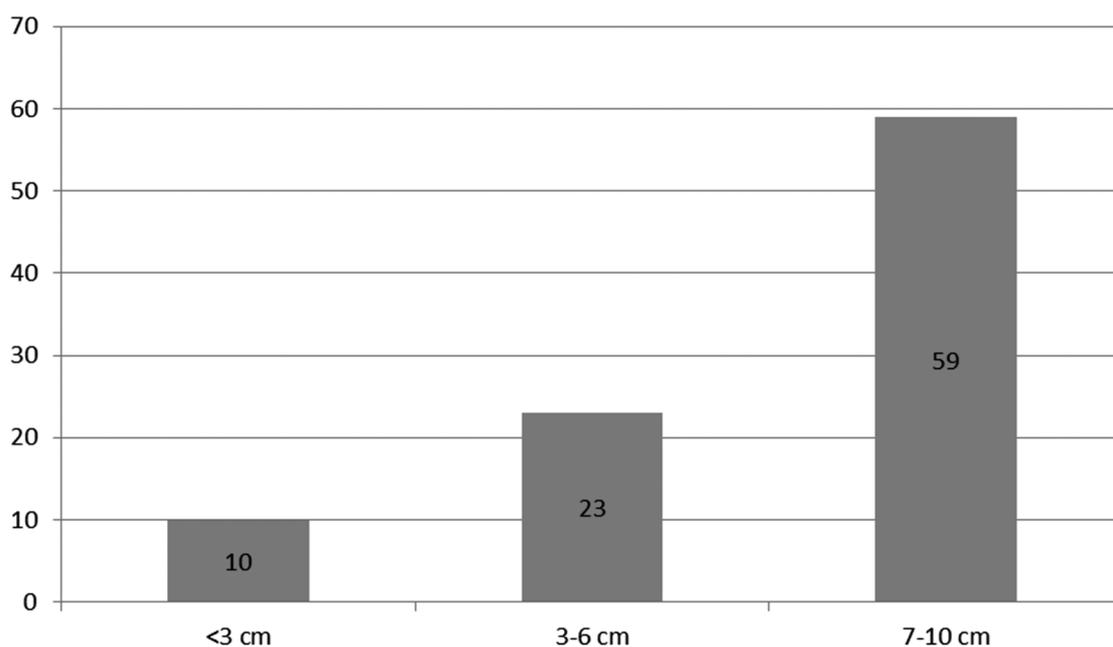
**Table 1.** The distance between the anastomosis and the pectinate line of the anal canal

Sample size	92
Lowest value	1,0000
Highest value	10,0000
Arithmetic mean	6,7609
95% CI for the mean	6,2770 to 7,2447
Median	7,0000
95% CI for the median	7,0000 to 8,0000
Variance	5,4587
Standard deviation	2,3364
Relative standard deviation	0,3456 (34,56%)
Standard error of the mean	0,2436

For practical reasons, we considered it appropriate to divide the group of patients who has undergone resection into three groups, according to the distance from the pectinate line of the anal canal: <3 cm (10 patients, representing 10.87%), 3-6 cm (23 patients, representing 25%) and 7-10 cm (59 patients, representing 64.13%) (Fig. 1).

Regarding the type of anastomosis, the results show that end-to-end anastomosis was performed in 33 patients (representing 35.86%), whereas in 59 patients (representing 64.13%) a side-to-end anastomosis has been performed.

During the surgical intervention, nervous elements were identified in 53 patients (57.6%), while in the remaining 39 patients (42.4%) they could not be objectively detected.



**Fig. 1.** The distance to which anastomosis has been made related to the pectinate line of the anal canal.

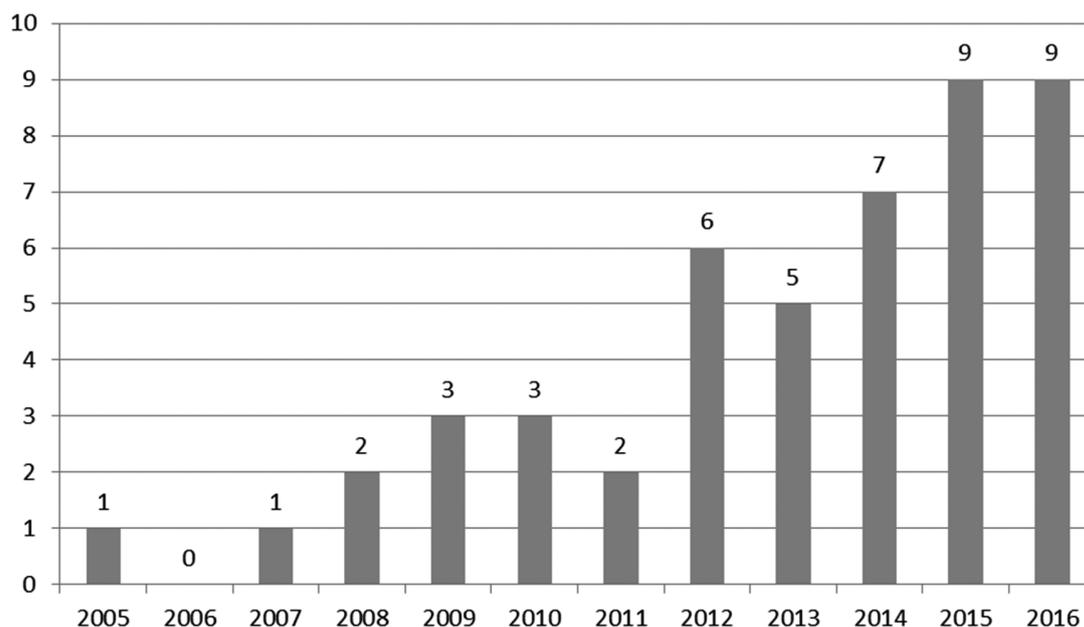


Fig. 2. Distribution of patients with temporary ileostomy with regard to the years

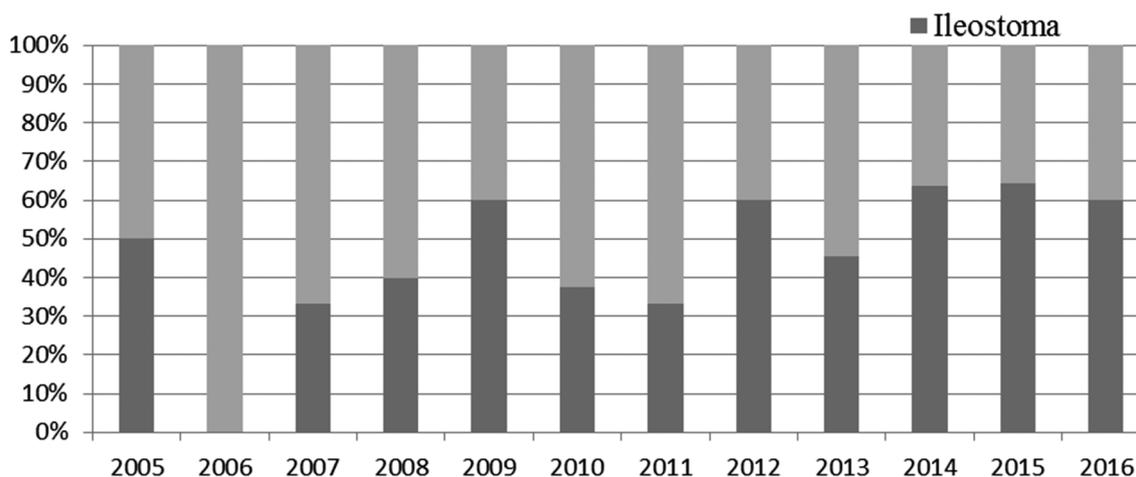


Fig. 3. Distribution of patients with temporary ileostomy in years

In the majority of patients with tumors located in the lower and middle rectum, protective ileostomy was performed. Thus, 48 patients (representing 52.17%) benefited from ileostomy during the 11 years of research. The evolution of this procedure shows an increase in the absolute value of the ileostomy (Fig. 2), with an approximately constant percentage value (Fig. 3).

During surgery, a series of intraoperative incidents and injuries was identified within the general group, the most common of which was difficult dissection (23 cases, representing 25%). In 17 cases (18.47%), tumor invasion determined the surgical team to perform associated hysterectomy.

Immediate postoperative complications within the general group were divided into local complications (62 cases, representing 38.27%) and general complications (18 cases, representing 11.11%). Of the local complications, the most frequent cases are intraperitoneal haemorrhage (22 cases representing 13.58%), parietal/perineal suppuration (14 cases, 8.64%) and anastomotic fistula (8 cases, 4.94%).

#### MORTALITY

In our research, we identified a total of 3 patients (1.85%) who died during admission due to complications that occurred postoperatively.

Taken into account the retrospective nature of the research, it became necessary to modify the LARS score so that it meets all of the following conditions: to be retrospectively calculated, to maintain its clinical significance, and to have a maximum of 42 points (Table 2).

**Table 2.** The LARS score adapted to be applied retrospectively

Complication	Answer	Points
Urgency	NO	0
	<1/week	11
	>1/week	16
Incontinence (can sum the points)	NO	0
	For gas	6
	For liquid	5
	For solid	10
Number of stools per day	>=4/day	4
	1-3/day	0
	<1/day	5

Summing up the points of each question, we found the total LARS score, calculated for the lot of patients with resections. Total score had values ranging from 0-42. The mean LARS scores in the study group were 12.46 with a median of 7 and a 13.06 standard deviation (Table 3).

**Table 3.** Statistical data on LARS scores

Sample size	92
Lowest value	0,0000
Highest value	42,0000
Arithmetic mean	12,4674
95% CI for the mean	9,7612 to 15,1736
Median	7,0000
95% CI for the median	4,0000 to 16,8754
Variance	170,7572
Standard deviation	13,0674

Percentage distribution of patients based on the LARS score reveals 36 patients (39.13%) with a score of 0 and a maximum incidence between 20-25 points for the rest of the patients (15 cases, representing 16.3%) (Fig. 4).

The numerical value of the LARS score does not always have a relevant clinical significance. As a result, the significance of the score value was divided into three categories: without LARS, with minor and with major LARS (Table 4)

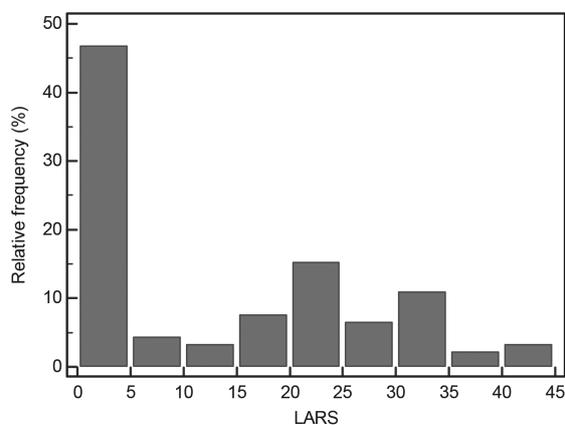
In the present research, we identified 57 patients (representing 61.96%) without LARS, 20 patients (representing 21.73%) with minor LARS and 15 patients (representing 16.31%) with major LARS (Fig. 5).

**Table 4.** The significance of the LARS score

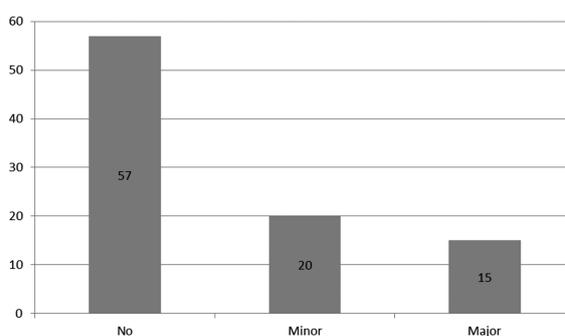
Significance	LARS
NO LARS	0-19
Minor LARS	20-29
Major LARS	30-42

The statistical analysis did not reveal significant correlations using the LARS score or its significance in the 3-grade division. But the occurrence of major LARS has shown numerous correlations with different quantified parameters in the research. Thus, 77 patients (representing 83.69%) did not have major LARS, while 15 patients (representing 16.31%) were classified as major LARS.

The distance to which the colorectal anastomosis was performed relative to the pectinate line of the anal canal was not a correlation factor with the LARS score (Pearson correlation coefficient  $r = -0,390$ ) (Table 8). In contrast, this parameter constituted, in our research, a predictive factor for the occurrence of major LARS (AUC = 0.847) (Figure 6). Thus, a distance of less than 3 cm between the pectinate line and the level of anastomosis, estimated intraoperatively, is a risk factor for the occurrence of specific postoperative disorders.



**Fig. 4.** Percentage distribution of patients based on the LARS score



**Fig. 5.** Distribution of patients according to the significance of the LARS score

The method of performing anastomosis, mechanical or manual, did not show a significant correlation with the LARS score for patients undergoing resection followed by anastomosis (Pearson Coefficient  $r = 0.374$ ) (Table 8). Achieving the ROC curve between the suture technique and the major LARS suggests a link between the two parameters, but without a strong correlation (AUC = 0.730) (Fig. 6).

In the case of the anastomosis type between the colon and the remaining part of the rectum, end-to-end or side-to-end, we could determine a significant correlation between this parameter and the LARS score (Pearson coefficient  $r = 0.510$ ) (Table 8), as much as between it and the occurrence of major LARS (AUC = 0.803) (Fig. 6). Thus, the end-to-end anastomosis predisposes the patients to the occurrence of late postoperative complications, with major implications for their lifestyle.

The use of the protective stoma in patients with rectal neoplasm, who have undergone surgical management consisting of previous resection, did not constitute, in our research, an element that would have a major influence on the LARS score ( $r = 0.265$ ) or the occurrence of major LARS (AUC = 0.667) (Table 8 and Fig. 6).

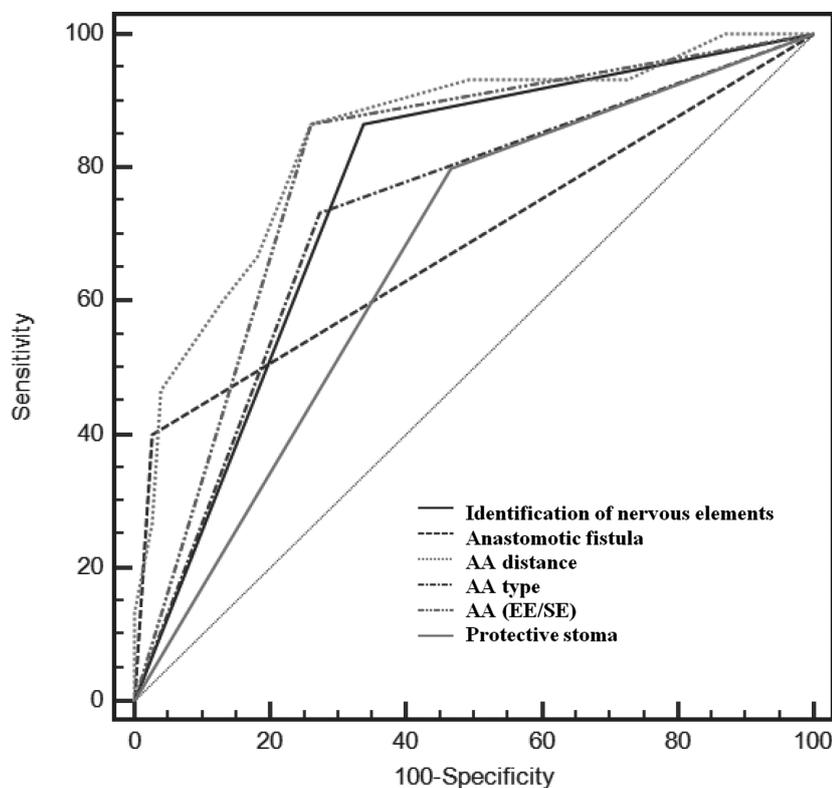
The identification of nervous elements during thorough dissection did not show a correlation value

with the LARS score (Pearson correlation  $r = -0.189$ ); instead, correlation of this parameter with the occurrence of major LARS revealed a very close relationship (AUC = 0.765) between the non-identification of nervous elements and the occurrence of major traumatic disturbances as a result of the surgery (Table 8 and Fig. 6).

Most postoperative complications did not show statistical correlations with the occurrence of LARS. However, the occurrence of anastomotic fistula was a parameter correlated with the LARS score for patients enrolled in the group of patients undergoing resection (Pearson Coefficient  $r = 0.469$ ). At the same time, the occurrence of fistula was also a risk factor for the occurrence of major LARS (AUC = 0.687) (Table 5 and Fig. 6).

**Table 5.** Pearson Coefficients

Parameter	Pearson coefficient
Distance AA- the pectinate line	-0,391
Type of AA (manual/mechanical)	0,374
AA (EE/SE)	0,510
protective stoma	0,265
Identification of nervous elements	-0,189
Anastomotic fistula	0,470



**Fig. 6.** Comparative analysis of ROC curves

## DISCUSSION

The possibility to practice a large number of colorectal anastomoses is also the aptitude of the modern methods of mechanical suture that have been used in our research in a number of increasing patients, reaching in 2016 a number of 6 patients, out of 15 who benefited from resection. The literature does not present data supporting the superiority of the mechanical suture over the manual suture, as confirmed by our research, from the fact that the mechanical suture did not correlate with the LARS score (Pearson coefficient  $r = 0.374$ ), and with the emergence of a major LARS has been correlated to a moderate extent, which may be considered a predictive factor for this pathological entity (AUC = 0.730).

The distance between the pectinate line and the anastomotic level has been shown to be a powerful predictive factor for the occurrence of major LARS. This distance varied between 1 and 10 cm with an average of 6.76 cm. The less than 3 cm value of this parameter correlated with the occurrence of major LARS (AUC = 0.847).

The type of anastomosis was also a factor that influenced the LARS score and the major LARS occurrence within the studied group. Thus, the end-to-end anastomosis performed in 33 patients predisposed to the development of a major LARS (AUC = 0.803). Side-to-end anastomosis, by obtaining a neorectal reservoir, reduces the incidence of postoperative digestive complications, such as incontinence or an increased number of faeces in 24 hours.

Identification of nerve plexuses during dissection was possible in 53 patients. This surgical maneuver had no impact on the LARS score (Pearson coefficient  $r = -0.189$ ), but non-identifying these elements constituted an important prediction factor for the occurrence of major LARS (AUC = 0.765).

Using a protective ileostoma with subsequent reintegration was identified in 48 patients. Taking into account the increasing number of resections related to amputations, the number of ileostomes increased yearly, from 1 in 2005 to 9 in 2016. Although the usefulness of such an ileostome is supported by numerous studies, especially for low anastomoses, in this research from the LARS development perspective we could not identify a particular importance regarding this procedure (Pearson Coefficient  $r = 0.265$  and AUC = 0.667).

Among incidents and intraoperative accidents, the highest frequency was identified in the case of difficult dissection (25%) and the need of proceeding hysterectomy during the same operative session (18.47%). None of these had any role in LARS.

With regard to the postoperative complications occurred in the evolution of patients, we have to

mention the anastomotic fistula with a frequency of 4.94% because the presence of this complication predisposes to some extent to the increased value of the LARS score (Coefficient Pearson  $r = 0.469$ ), as well as to the occurrence of major LARS (AUC = 0.687).

LARS score values ranged from 0-42 points, with over 45% of cases in the range 0-5 points. For practical reasons, we have quantified the occurrence of major LARS as a marker of severity of postoperative evolution in patients with rectal neoplastic disease. Thus, a total of 15 patients developed major LARS, while 77 patients showed minor LARS or did not have LARS. All of this LARS score data are consistent with the data identified in the literature on this subject.

## CONCLUSIONS

1. The type of anastomotic suture (mechanical/manual) did not significantly influence the occurrence of LARS, and its evolution over time has not shown superiority of mechanical anastomosis versus manual anastomosis.
2. The distance from the anastomosis level to the pectinate line of the anal canal was a predictive factor for the LARS appearance, especially in the case of values below 3 cm.
3. Side-to-end anastomosis is preferred, because it is an element that improves the probability of not developing major LARS post-surgery.
4. Non-targeting the nervous plexus constituted a predictive factor for the development of major LARS.
5. Creating a protective ileostomy did not influence the LARS score, but predisposes to the occurrence of major LARS.
6. The occurrence of anastomotic fistula is a predictive factor of the occurrence of major LARS during post-surgery evolution.
7. The LARS score demonstrates its validity in the Romanian population, the data recorded during the study being consistent with the literature.
8. Implications with regard to social integration and quality of life in patients with this type of illness further emphasize the importance of patient involvement in the therapeutic decision by obtaining informed consent in written form.

### Authors contribution

All the authors have equal contribution to this paper. All authors approved the final version of the manuscript.

## REFERENCES

1. Peng LC, Milsom J, Garrett K et al. Surveillance, epidemiology, and end results-based analysis of the impact of preoperative or postoperative radiotherapy on survival outcomes for T3N0 rectal cancer. *Cancer Epidemiology* 2014; 38(1) : 73-78.
2. Hötter AM, Garcia-Aguilar J, Gollub MJ. Multiparametric MRI of rectal cancer in the assessment of response to therapy: a systematic review. *Diseases of the Colon and Rectum*, 2014; 57 (3): 790-799.
3. Park IJ, You YN, Agarwal A et al. Neoadjuvant treatment response as an early response indicator for patients with rectal cancer. *Journal of Clinical Oncology*, 2012; 30(8): 1770-1776.
4. Martin ST, HM Heneghan, Winter DC. Systematic review of outcomes after intersphincteric resection for low rectal cancer. *British Journal of Surgery*, 2012; 99(9): 603-612.
5. Ion D, Stoian RV, Păduraru DN, Bolocan Alexandra, Șerban MB. Certitudes and controversy regarding neural elements preservation in ETM (Total Mesorectal Excision) technique. *Chirurgia*, 2012; 107(2): 231-236.